

Serial No. 10/010,645

Amdt. dated November 18, 2004

Reply to the Office Action of August 19, 2004

REMARKS

The Office Action mailed August 19, 2004, has been received and reviewed. Claims 49, and 51-61 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being vague. Claims 54-61 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description. Reconsideration is respectfully requested.

Rejections under 35 U.S.C. § 112, second paragraph:

Claims 49, and 51-61 stand rejected under 35 U.S.C. § 112, second paragraph, as assertedly being vague. While the applicants respectfully disagree, independent claims 49 and 54 have been amended to clarify the meaning of "associated therewith," "administering" and "infecting." In particular, "associated therewith" has been replaced with a recitation that the fiber protein is a part of the capsid of the recombinant adenovirus (*i.e.*, associated therewith), and that "administering" encompasses "infecting" the cells. As suggested by the Examiner, the claims have been amended to remove the redundancy of the "administering" and "infecting" terms.

Specifically, the amendments clarify that the nucleic acid is delivered through infection of the cell by a recombinant adenovirus and that the fiber is associated with the capsid of the recombinant adenovirus. Therefore, the amendments should remove the perceived vagueness issues in the pending claims. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejections under 35 U.S.C. § 112, first paragraph:

Claims 54-61 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking sufficient written description. The Office asserts that there is insufficient description of the "knob regions" (page 4 of the Office Action). The applicants respectfully disagree.

The Office acknowledges that the specification teaches that fiber proteins from adenovirus serotypes such as 16, 35, 40-S and 51 (*Id.*) provide tropism for mesenchymal stem cells. The specification also teaches the trimeric structure of the fiber protein, *i.e.*, the tail, stem, and knob regions. The specification further teaches that the tail region, for example, the

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conserved FNPVYP sequence, is involved in anchoring the fiber to the penton base and that the knob region is responsible for initial interactions with the cellular adenovirus receptor (*see*, for example, paragraphs 24 and 40). In addition to the teachings of the specification, the structure and function of the three regions was known in the art. Hence, a person of ordinary skill in the art knew that they could swap the fiber knob region once they knew that a particular fiber provided a desired tropism (*see*, for example, Krasnykh *et al.* 1996 (previously submitted); and Stevenson *et al.* 1995 and 1997¹ (courtesy copies provided herewith)). In particular, Stevenson 1997 states in the abstract "that exchange of the fiber head [knob] domain is a viable approach to the production of adenovirus vectors with cell-type-selective transduction properties," Stevenson *et al.* (1997) Selective Targeting of Human Cells by a Chimeric Adenovirus Vector Containing a Modified Fiber Protein, *J. Virol.* 71(6):4782-4790, 4782.

A "patent specification is not intended nor required to be a production specification" (MPEP § 608.01(h)). "Furthermore, a patent need not teach, and preferably omits, what is well known in the art" *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986) (*citing Lindemann Maschinenfabrik v. American Hoist and Derrick*, 730 F.2d 1452, 1463, 221 USPQ 481, 489 (Fed. Cir. 1984)). Hence, the present specification is not required to provide a step by step production outline for exchange of a knob domain, since this information is well known in the art. In the present case, when combined with the knowledge of a person of ordinary skill in the art, the instant specification provides a written description of the correlation between the knob region of a fiber protein and tropism. For example, Krasnykh *et al.* (of record), which is cited in paragraph 40, discloses the generation of a recombinant fiber protein wherein the knob domain from Ad3 replaces the knob domain of Ad5. In addition to Krasnykh *et al.*, Stevenson *et al.* '95 and Stevenson *et al.* '97 demonstrate that a person of ordinary skill in the art is able to produce a functional chimeric fiber protein using the

¹ While the Stevenson *et al.* '95 and Stevenson *et al.* '97 references are not considered more relevant than the references considered by the Patent Office, for example, Krasnykh *et al.* 1996, they do demonstrate that a person of ordinary skill in the art knows of the correlation between the structure and function of the knob domain.

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knob domain of a second subgroup. Hence, a person of ordinary skill in the art knows the correlation between the various regions of a fiber protein and their respective function.

Further, vector pBr/Ad.BamRΔFib (*see*, paragraph 72) utilizes a NdeI site in the sequence encoding the Ad5 fiber tail. This vector does not replace the sequence upstream of this NdeI site. Only the sequence downstream is replaced, which encodes part of the tail, the stem and the knob region. Hence, these examples demonstrate (reduce to practice) chimeric fiber proteins, not complete deletion and replacement of the "entire adenovirus 5 fiber sequence" as stated in the Office Action (page 4 of the Office Action). The applicants used this construct to generate over 30 chimeric fiber proteins (*see*, paragraph 74 and 75).

Furthermore, the materials and method section of Krasnykh *et al.* (1996) *J. Virol.* 70(10):6839-6846, 6840 (of record), cited in paragraph 40, which discusses the various regions of the fiber protein and their function (the structure function relationship of the fiber protein), demonstrates another more labor intensive method of exchanging a knob region. While the Krasnykh *et al.* method is simply to labor intensive to allow the production of over 30 chimeric fiber proteins, it and other references demonstrate that a person of ordinary skill in the art, using the guidance of the instant specification, understands the correlations between structure and function, specifically, the knob, stem and tail structures and their respective functions.

Hence, a person of ordinary skill in the art would recognize the thirty plus examples of chimeric fiber proteins provided by the specification, having different knob domains, as demonstrating that the applicants were in possession of the claimed genus at the time of filing. The production of over 30 fiber constructs provides a description of a representative number of species.

Thus, the applicants submit that claims 54-61 have more than sufficient written description. Reconsideration and withdrawal of the rejection are respectfully requested.

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CONCLUSION

Claims 49 and 51-61 should now be in condition for allowance, early notification of such is respectfully requested. Should questions remain after entry of the amendments and consideration of the remarks herein that may be resolved by a telephone conference, the Examiner is invited to contact the applicants' representative at the number provided herein.

Respectfully submitted,



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